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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/867,536	05/31/2001	Juerg Gysin	206397US0X	7147

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	8

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/867,536	GYSIN et al.
Examiner	**Art Unit**
James L. Grun, Ph.D.	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *13 Nov 2003*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above, claim(s) *3-9, 14, and 16-23* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 10-13, and 15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *31 May 2001* is/are a) ☐ accepted or b) ☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1641.

Applicant's election with traverse of Group I, claims 1, 2, 10-13, and 15, in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the Office has provided insufficient reasons or examples of patentable distinctness of the inventions as grouped and that searching all of the claims together would not be burdensome. This is not found persuasive because the explanations of different structures, functions, method designs, method performance, classifications, and fields of search made in the restriction requirement of record are sufficient to provide a *prima facie* showing of a serious burden upon the examiner.

This application has been filed with informal drawings which are acceptable for examination purposes only. Applicant is required to submit corrected drawings acceptable for publication within the time period set in the Office action. See 37 CFR 1.85(a). Submission of corrected drawings may no longer be held in abeyance pending the indication of allowable subject matter. Failure to take corrective action within the set period will result in **ABANDONMENT** of the application. Direct any inquiries concerning drawing review to the Drawing Review Branch at (703) 305-8404.

The disclosure is objected to because of the following informalities: page 1, line 22, it is believed that --PfEMP-1-- was intended; page 2, line 5, it is believed that --trophozoites-- was intended; page 5, line 5, it is believed that --stage-- was intended; page 16, line 6, it is believed that --then-- was intended; page 16, line 7, it is believed that --erythrocytes-- was intended; page 18, line 10, it is believed that --investigated-- was intended; the brief description of drawings 1-3, and all reference to said drawings in the specification must indicate the panel of the Figure which is described or to which the reader is being referred, e.g. the Figures should be described and cited as Figure 1A or 1B or 1C or 1D, or Figure 2A or 2B, or Figs. 3A-3E; in this regard, page 20 references a non-existent Fig., i.e. Fig. 3F. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1, 2, 10-13, and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There is nothing in evidence which would assure one that either of the proteins identified merely by approximate molecular weight and reactivity with applicant's undefined polyclonal antisera has any function in ring-stage adhesion of erythrocytes infected with certain selected parasite phenotypes to certain endothelial cells as is instantly disclosed and claimed. Applicant teaches that apparently indistinguishable proteins are found on the surface of both adhesive and non-adhesive infected erythrocytes (see e.g. page 22). Thus, surface presence or absence of the instant proteins does not correlate with and appears irrelevant to adhesion or non-adhesion, respectively. The capability of these proteins to be surface ^{125}I-labelled would not be dispositive of any question regarding adhesive binding function if the same proteins can be similarly labelled on adhesive and non-adhesive infected erythrocytes. Applicant also presents the mere implication that antibody binding to the disclosed proteins inhibits adhesion. Applicant's undefined polyclonal antisera bind many parasite proteins, thus the evidence that such antisera inhibit infected erythrocyte adhesion points to no particular antigen-antibody reaction using these antisera because the inhibitory activity may be the result of binding of polyclonal antibodies in the antisera to any number of parasite proteins. Moreover, many labelled proteins appear to be immunoprecipitable and enzyme sensitive from labelled infected erythrocyte extracts with applicant's undefined polyclonal antisera (see e.g. Fig. 3b) and therefore any factual basis, absent more, to support applicant's

suggestion for any functional role of the proteins is not clear. Further, it is not assured that one could obtain such proteins in isolated form with such molecular weights (and which also function in the invention, see above) without applicant's antisera. Apparently many proteins of similar molecular weight are present even in uninfected erythrocytes and applicant's antisera appear required to distinguish and/or isolate certain parasite proteins from those of normal erythrocytes. Absent further written description and guidance from applicant, and further unguided experimentation, the ability of any particular polyclonal antisera to bind the relevant antigens would seem unknown and therefore unpredictable for any one other than applicant to predictably and repeatedly obtain any of the disclosed proteins. Note that the methods for preparing all required reagents must be publicly known as of the application filing date. Ex parte Moersch 104 USPQ 122. For the reasons set forth above, absent further written description, guidance, and undue experimentation, one would not be assured of the ability to predictably obtain and use any isolated proteins as instantly disclosed and claimed.

Claims 10-13 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant provides no guidance for any nexus between detection of anti-"RSP" antigen antibodies in a patient with diagnosis of disease due to malarial parasite infection (i.e.

malaria) in that patient, particularly for diagnosis of an active "ring-stage" infection. At best, the prior art would suggest that antibodies specific for a multitude of antigens of malarial parasites are elicited in naturally-infected patients and may simply reflect prolonged exposure in areas endemic for malarial parasite transmission. There is nothing in evidence that a single or even an active infection elicits or augments antibody detectably reactive with these antigens. Thus, the specification fails to provide an adequate written description of the invention and is not enabling for the diagnosis of malaria merely by determination of anti-"RSP" antigen antibodies. Moreover, many malaria infections would be expected to occur in the absence of detectable anti-"RSP" antigen antibodies and many such malaria infections would not be detectable with such a method. Thus, in the absence of further written description and guidance from applicant, detection of antibodies specific for the "RSP" antigen of malarial parasites is indicative only of past exposure to the malarial parasites and is not diagnostic of current, or even recent, episodes of malaria, and, conversely, a lack of detectable antibodies would not indicate lack of infection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 10-13, and 15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "approximately" in the claims is a relative term which renders the claims indefinite. The term "approximately" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is believed that --molecular weight-- rather than "size" was intended in the claims.

In claims 10-13, recitations of "the presence" lack antecedent basis. It is not clear what is being determined by the method because the preamble recites "presence of a Plasmodium antibody" and the body of the claims recites "presence of the Plasmodium."

In claim 15, it is not clear what is being determined by the method of the claim because the preamble recites "diagnosing...blood-stage cycle" and the body of the claim recites "indicates a ring-stage infection."

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 2 is rejected under 35 U.S.C. § 102(b) as being anticipated by Saul et al. (U.S. Pat. No. 5,573,943) in light of Douki et al. (Blood 101(12): 5025, 2003).

Saul et al. disclose the RAP-2 protein which, in light of Douki et al. (page 5028, col. 2), inherently is the instant approximately 40 KDa RSP-2 protein.

Claims 2, 10-13, and 15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Stowers et al. (Inf. Imm. 65(6): 2329, 1997) in light of Douki et al. (Blood 101(12): 5025, 2003).

Stowers et al. disclose isolated recombinant and parasite-derived RAP-2 protein which, in light of Douki et al. (page 5028, col. 2), inherently is the instant approximately 40 KDa RSP-2 protein. The protein preparations were used for the detection of antibodies in samples from patients.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone numbers for official facsimile transmitted communications to TC 1600, Group 1640, are (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

James L. Grun, Ph.D.
March 5, 2004

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641